Serial No.: 10/778,010
Filing Date February 11, 2004

REMARKS

Claims 1-6 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sherrington, et al. in view of Barretto, et al. The Examiner states that it would have been obvious to use the layering of Barretto and Sherrington because Barretto, et al. discloses the use of multiple layering particles which allows more control over the column capacity and improves such capacity.

The claims recite flow-through ion exchange medium which comprises a monolithic stationary phase having interconnecting pores defined by pore walls and fine ion exchange polymeric layering particles irreversibly bound to the pore walls. Advantages of this medium are cited in detail in paragraphs [0044] through [0046] of the present application. It provides an ability to control capacity and selectivity through optimal choice of the monolithic phase and the layering particles. It further leads to a reproducible medium. Further, due to the uniformity of the coating process, high efficiencies are possible.

Barretto only disclose the use of layering particles on particulate substrates (beads) for bead beds. Such beads are fundamentally different from the monolithic substrate of the present invention. In an analytical column packed with beads coated with layering particles, the significant portion of the liquid flow is through the interstices volume unoccupied by the beads, rather than flowing through the pores of the beads. In contrast, in a monolithic phase, the monolith pores are the only available flow path and so the entire liquid flow path is through the pores. The flow profile through monolithic pores is fundamentally different than flow through the interstices between the particles of the Barretto approach. Due to the flow through the pore the mass transfer properties are improved for the monolithic phases particularly at high flow rates

Another advantage of the invention is shown at paragraph [0009] of the present specification. The Barretto approach leads to potential difficulty in uniformly packing the column with smaller beads with higher packing density. In contrast, a monolithic column substrate can be uniformly layered with layering particles and hence allows effective reduction in HETP and improves separation efficiencies.

A further advantage, shown in paragraphs [0009] and [0010] of the present specification, is that high flow rates are possible with monolithic columns leading to higher efficiencies in comparison to packed columns of Barretto.

Furthermore, as set forth in the specification, the use of monolithic phases of the prior art requires stringent control of conditions during manufacturing to achieve reproducible performance during chromatography. The present invention provides an elegant solution to this scale up and reproducibility problem by including the functionality in the small layering particles on the monolithic wall. A single batch of the layering particles is sufficient for a large number of columns thus ensuring reproducible separations, column to column.

Sherrington discloses a medium used for peptide synthesis, not for analytical scale chromatography. All examples in Sherrington use milled or ground and sieved powder having a particle size of 250 to 1500 μm. The disclosure in Sherrington of suitable porous materials for use as the Sherrington substrate are those described in U.S. Patent No. 4,522,953. (Sherrington, Col. 4, line 48.) Such porous substrates of the '953 patent were made by a process termed high internal phase emulsion (HIPE). However, HIPE polymers are not suitable for binding to a gel of the type described in Sherrington or with polymeric layering particles of the type claimed herein. This is clear from a subsequent U.S. Patent No. 6,100,306. At Col. 2, lines 16-38, the '306 patent states (1) that HIPE polymers produce a block of polymer material the size and shape of the vessel used for polymerization; (2) it is very difficult to wash unpolymerized emulsion components out of the block; (3) the material can only be used by grinding the block into particles which is costly; (4) the size of the particles are limited; (5) removal of residual emulsion components is essential for many applications; and (6) no cost effective method for performing this wash step to remove the emulsion has been developed. This patent was long after Sherrington.

Without washing the unpolymerized emulsion, such components would remain in the pore of the block. This would create massive back pressure and likely would lead to significant errors in chromatography results as the emulsion components are displaced during a chromatographic run.

An additional problem with such prior art HIPE polymer blocks is that the blocks have skins that form at the interface between the HIPE and the container used for polymerization. See, e.g., U.S. Patent No. 4,522,953 at Col. 4, lines 1-6. To produce a permeable block for chromatography, the skin must be removed.

From the foregoing, it is clear that a monolithic phase of HIPE polymer is the only one disclosed in Sherrington, is not operable. Grinding the phase results into particles faces the problems outlined in the present application.

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Because the residual emulsion components fill up the pores of HIPE polymer blocks of Sherrington, this would inhibit the ability to the Sherrington gel to fill the pores of Sherrington since the pores are already filled. Moreover, the emulsion would inhibit binding the polymer layering particles of the present invention.

Referring the first paragraph on page 3 of the Office Action, the second reference to a monolith in Sherrington is not more extensive than the first. It provides no support for a method of making the monolith or for filling it with gel. The remainder of the Sherrington disclosure refers to the use of particles as the substrate.

Referring to the third paragraph on page 3 of the Office Action, the Examiner recites a comment at Col. 6, lines 25-32, of Sherrington to suggest the gel causes negligible pressure development. However, all of the disclosure of the specific embodiment of Sherrington refers to a polymeric material which is in the form of a milled and sieved powder. That back pressure statement precedes the examples in which such polymeric substrates are disclosed. For the reasons set forth above, Sherrington teaches no practical way to use a monolith as the substrate for the gel. This is crystal clear by the statements from the '306 patent discussed above.

Referring the fourth paragraph on page 3 of the Office Action, there is a fundamental difference between Sherrington and the present claims in terms of the monolith. Sherrington does not disclose how to bind the gel to the pores of a monolith. Even if it did, the HIPE polymer, which includes the emulsion precursor set forth in the '306 patent, would create massive back pressure, assuming that the product could be made at all in using a monolith substrate in view of the pores being filled with the emulsion.

Referring to the paragraph bridging pages 3 and 4 of the Office Action, the teaching of Barretto for improved control over column capacity is in the context of a resin bed packed with beads. The improvement relates to beads. There is no motivation shown in Sherrington for improvements in a monolithic substrate. There is no suggestion of improving a monolith including a gel by the use of beads.

In view of the foregoing, it is submitted that the claims are in condition for allowance. Favorable action is solicited. If the Examiner has any questions, please direct any calls in to the undersigned at (415) 781-1989.

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The Commissioner is authorized to charge any additional fees which may be required, including extension fees or additional claim fees, or credit any overpayment, to Deposit Account No. 50-2319 (Our Order No.: 465377-01102; Our Docket No.: 33568/US).

Respectfully submitted,
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Dated: 6/30/06

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